GUTS, BUGS, AND DIETARY FIBER

Investigating the colon-diet-flora system using modeling and simulation

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OVERVIEW

- ► How diet impacts gut microbiota, and subsequently, how microbiota affects health, has been a topic of significant discussion for the past several years?
- Many hypotheses relating microbiota state to health concerns are prevalent:
 - neural developmental disorders (autism spectrum)
 - anxiety and depression
 - obesity
 - cancer

OVERVIEW

- ► The human colon is inherently difficult to investigate *in vivo* due to its physical inaccessibility.
 - Assessment is usually done using only the materials entering the digestive system through diet or exiting as feces.
- Large variability exists in microbiota composition between individuals and within a single person, posing clinical challenges.

OVERVIEW

Experimental Tool	Microbial Ecology	Host Phys- iology	Experimental Control	Cost ^A	
Clinical Trials	X	X	limited	very high	
Animal Models	X	X	moderate	high	
Reactor Systems	Х		high	moderate	
Mathematical	Х	Х	complete	low	
Models ^B					

A: Cost includes financial considerations, as well as ethical concerns and experimental time.

B: Mathematical models will often focus on either microbial ecology or host physiology to ensure models maintain analytical value.

RESEARCH OBJECTIVES

To design and develop a widely accessible software tool(s), grounded in physical modeling and deterministic approaches, to aid in exploring mechanical aspects of colon-diet-flora behavior through supporting the rapid design, execution and analysis of simulation experiments.

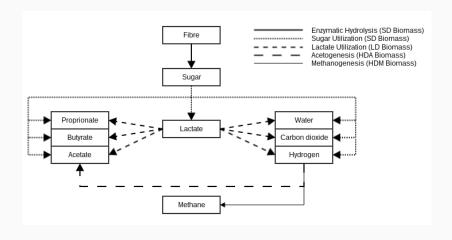


http://compugut.sourceforge.net

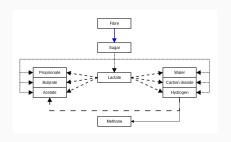
MATHEMATICAL FORMULATION



MODEL



Model



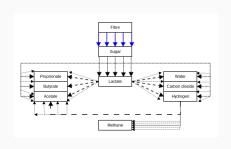
$$\phi_h = \mu \frac{F}{KX + F} X$$
 (1)
$$\phi_f = \mu \frac{S}{K + S} X$$
 (2)

$$\phi_f = \mu \frac{S}{K + S} X \tag{2}$$

Model

1013	soluble components		2	-	,	-		-			W
	Component i	1	2	3	4	5	6	7	8	9	Kinetic Rate
Pr	Process	S ₁	S ₂	S ₃	S ₄	S ₅	s ₆	S ₇	58	S ₉	
1	Hydrolysis	Y _{1,1}									$\phi_1(c)$
2	Glucose utilization	-1	Y _{2,2}	Υ _{3,2} Υ _{3,3}	Y _{4,2}	Y _{5,2}	Y _{6,2}		Y _{8,2}	Y _{9,2}	$\phi_2(c)$
3	Lactate utilization		-1	Y3,3	Y _{4,3}	Y _{5,3}	Y ₆ ,3		Y8,3	Y9,3	$\phi_3(c)$
4	Homoacetogenesis			-1	Y4,4				Y8,4	Y9,4	$\phi_4(c)$
5	Methanogenesis			-1				Y _{7,5}	Y _{8,5}	Y _{9,5}	$\phi_5(c)$
For p	particulate components										
	Component i	10	11	12	13	14	Kinetic	Rate			
j	Process	11	<i>X</i> ₁	Х2	Х3	X ₄					
1	Hydrolysis	-1					$\phi_1(c)$	$= \kappa_1 \frac{I_1}{K_1 X_1}$	$\frac{x_1}{1+l_1}$		
2	Glucose utilization		Y _{11,2}				$\phi_2(c)$	$= \kappa_2 \frac{S_1}{K_2}$	½ ₁ -S₁		
3	Lactate utilization			Y _{12,3}			$\phi_1(c)$ $\phi_2(c)$ $\phi_3(c)$ $\phi_4(c)$ $\phi_5(c)$	$= \kappa_3 \frac{\xi_2}{\kappa_2}$	X2 +52		
4	Homoacetogenesis				Y _{13,4}		$\phi_4(c)$	$= \kappa_4 \frac{\varsigma_3}{\kappa_2}$	X ₃ ² ⊢S ₂		
5	Methanogenesis					Y _{14,5}	$\phi_5(c)$	$= \kappa_5 \frac{S_3}{V}$	X ₄ I _S -I _{DH}		
						,=		(ex	p(— 3(ph	$\frac{-pH_U}{(1-pH_U)^2}$	if $pH < pH$ if $pH \ge pH$
							with Ip	4 = { . '	` `рн	J-bHF,	
6	Dosay of V		-1								ітрн ≥ рн
	Decay of X ₁		-1	1				$= \kappa_{6,1} X_1$			
7	Decay of X ₂			-1				$= \kappa_{7,1} X_2$			
8	Decay of X ₃				-1			$= \kappa_{8,1} X_3$			
9	Decay of X_{L}					-1	$\phi_{\alpha}(c)$	$= \kappa_{9.1} X_L$			

MODEL



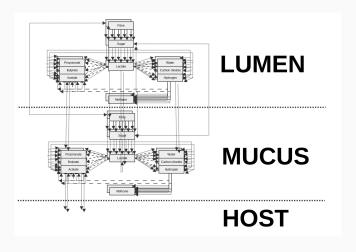
$$P_{i,j} = \mathcal{N}(P_i, \sigma)$$

$$\phi_h = \frac{F}{F + \sum_{i}^{n} K_i X_i} \sum_{i}^{n} \mu_i X_i \qquad (3)$$

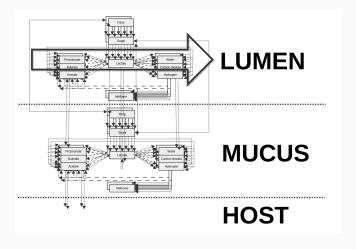
$$\phi_f = \sum_{i}^{n} \mu_i \frac{S}{K_i + S} X_i \qquad (4)$$

$$\phi_f = \sum_{i}^{n} \mu_i \frac{S}{K_i + S} X_i \qquad (4)$$

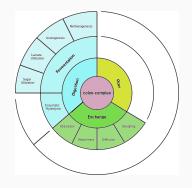
Model



Model



MODEL



$$\partial_t \mathbf{c} + \partial_x f(\mathbf{c}) = r(\mathbf{c}) + e(\mathbf{c})$$
 (5)

where **c** = concentration of materials in the colon-complex

- 1. sugar
- 2. lactate
- hydrogen
- 4. acetate
- 5. propionate
- 6. butyrate
- 7. methane
- 8. carbon dioxide

- water
- 10. fiber
- 1. sugar utilizing biomass
- 2. lactate utilizing biomass
- 3. acetogenic biomass
- 14. methanogenic biomass

MODEL

System Details

Process Model: colon-complex (diet-flora-colon)

Sub-processes: 3

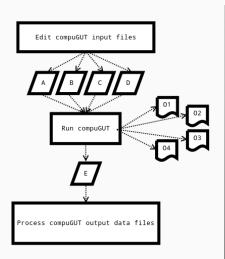
Number of State Variables: 28-100

Biochemical Parameters (BP): 34

Spatial Exchange Parameters (SEP): 56

Physical Parameters (PP): 10

Operation Parameters (OP): 9



A = Operation Instructions

B = Diet Specifications

C = Inoculation Conditions

D = ADM1 Parameters

O1 = Simulation Summary

O2 = Simulation Parameters

O3 = Recorded Time Values O4 = Colon Input Fiber v Time

E = Output Data Files

```
compuGUT: Operation Instructions
# Created: June 28th, 2014
# Simulation Type:
1.0
                p0 - Simulation Type (1: continuous, 2: 3-stage, 3: gradostat, 4: All [for comparison])
# Sizing and Operation Parameters:
                                        Values from www.webMD.com (Jun 28, 2014)
1.524
                pl - Length of colon [m]
                                                        ~ 5 feet in average human
0.0762
                p2 - Average diameter of colon [m]
                                                        ~ 3 inches in average human
                                                       ~ 20 feet in average human
5.096
                p3 - Length of small intestine [m]
0.0254
                p4 - Average diameter of SI [m]
                                                        ~ 1 inch in average human
7.0
               p5 - Average Flow rate [lpd]
28.0
               p6 - Simulation Run Time [d]
# Microbial System:
1.0
                p7 - Number of representative sugar degrading biomass species
1.0
                p8 - Number of representative lactate degrading biomass species
1.0
                p9 - Number of representative Hydrogen degrading acetogenic biomass
                p10- Number of representative Hydrogen degrading methanogenic biomass
1.0
                pll- Level of variance in which biological parameters may exist
# Sensitivity/Stability Parameters:
                p12- Level of variance in which physical operations can exist
# Computing Parameters:
                p13- Grid Resolution
A A
10
                pl4- Number of Iterations between output save
"user operation instr compuGUT.txt" 29L. 1182C
```

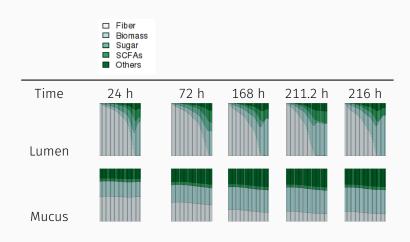
```
compuGUT: In silico platform for simulation of intestinal fermentation
Version: 0.1.0
Copyright: 2015 Moorthy & Eberl

Problem Size: 28 x 51
System Flow Rate [L/d]: 7.000000
Convective velocity [m/d]: 1.534964
Colon Volume [L]: 6,950000 (0.973000 + 1.946000 + 4.031000)
Small Intestine Volume [L]: 3.008889
delx = 0.030480 [m]
delt = 0.019857 [d]
Simulating colon:
Done!
```

```
compuGUT fm Simulation Summary:
Date and time: Fri Apr 3 23:38:01 2015
Simulation Type: Continuous Colon Model
Number of State Variables: 28
Number of Sugar Degrading biomass: 1
Number of Lactate Degrading biomass: 1
Number of Acetogenic biomass: 1
Number of Methanogenic biomass: 1
Bioparameter variance: 0.000000
Grid resolution: 51
Length of simulated colon [m]: 1.524000
Average diameter of colon [m]: 0.076200
Average flowrate [L/d]: 7.000000
Days simulated: 28.000000
Computing time [s]: 190.610001
Number of output files created: 1411
Contact Arun [amoorthy@uoquelph.ca] or Hermann [heberl@uoquelph.ca] with questio
ns or feedback
(c) Moorthy and Eberl, 2015
SimulationSummary.txt (END)
```

ise: 11.2	18423														
664377	0.427779	6.000020	0.027543	0.00000	0.000002	0.000036	2.498972	0.000000	2.236266	0.000011	3.134333	0.000001	0.221401	6.600000	1.0020
000020	44.233522	14.200595	24.985995	0.013742	31.765666	0.000002	15.488376	0.000129	0.207632	0.011449	29.859225	0.000003	A 130044	0.000020	1 7000
000051	44.216147	14.402583	24.000377	8.641227	33.334669	0.020405	15.500119	0.000388	0.295189	0.034348	26.898729	0.000011	9.239777	0.000004	1.700
031903	0.100503 44.215488	0.000008	0.000704 24.029534	0.000000 0.000000	0.000002	0.000000	2.477522	0.000200	2.218241	0.000300	3.110072	0.000033	0.339677	0.000298	1.7000
070437	0.100143 44.272588	0.001300	0.000700 26.796353	0.000000 0.123500	0.000002 33-690736	0.001111	2.401240	0.000040	2.771100 0.317505	0.000843	3.114414	0.000074	0.229908	0.000000	1.7930
162711		0.002220				0.002207		0.001700		0.001040		0.000143	0.220443	0.001274	1,794
002911	0.200422	13.943053	24.767630 6.606711	0.151200	31.569391	0.074538	15.641510	0.003584	0.335000	0.125793	24.266663	0.000343			1,799
001026	84.066134	13.000007		0.170058	31.457139	0.000004	14.494722	0.001884	0.332584 7.738556	0.141825	24.333004	0.000343	6.77778	6.662301	1 8854
			8.800718 24.672489												
.190304	0.500012	0.007137	6. 626723 24. 477424	0.000001	0.000002	0.000779	7.511120	0.003393	7.745489	0.000037	3.149395	0.000373	0.222548	0.004995	1.0121
												0.000007	0.222472	0.000078	1.0190
034838	64.055554	11.003104	24.570000	0.243504	31.075396	0.120100	2.553522	0.002754	0.355655 7.765333	0.210000	24.672366	0.001002	0.224512	0.009295	1.000
023113	45.170047 8.384343	10.033061 6.033065	24.514720 6.626728	0.292377	32.099710	0.143145	10.034721	0.003087	0.362536 2.275465	0.242787	26.666117	0.001434	0.225673	6.612252	1.037
329797	0.584110	0.014932	0.026724	F. 600005	0.000002	0.027962	2.563334	0.018488	2.288739	0.022737	3.200571	0.001833	0.226548	0.015559	1.8488
362656	0.583350	6.65669 6.730300	0.026717 24.327130	0.000000 0.200000	8.808082 32.314083	0.034864	2.577213	0.003381	2.302034	0.020612	3.227154	0.002284	0.228337	0.019323	1.859
												0.002795	0.222020	0.023542	1,472
.000313	40.302031	9.999374	24.220462	8.411841 8.606662	32.005543	0.200047	2,512628	0.004187	0.292329	0.341004	27.207876	0.003354	0.221415	0.020220	1.000
457900	0.500304	0.020005	0.024668	0.000002	0.000002	0.068797	2.631727	0.042188	2.347924	0.051054	3.299721	0.003003	0.233300	0.033385	1.000
181824	0.679178	0.022360	0.020543 24.042043	0.000002	0.000002 22.149427	0.073100	2.652654	0.040650	2.364888	0.060163	3.335000	0.004677	0.234953	0.030000	1.6111
												0.005417	0.337623	0.041018	1.6360
.138338 .547626	47.928434	9.477477	0.026378	0.536243	33.338597	0.202147	2.702827	0.000007	0.421790 2.405799	0.444031	37.623047	0.001212	0.220267	0.051500	1,040
135366	48.434787	5.455141 6.624316	23.897666 0.626338	8.568665 8.606662	9.000002	0.278879	2.732839	0.000478	0.429053 2.429025	0.471456	27,700488	0.007020	0.242000	0.000220	1.070
171814	0.073410	0.021617 5.176882	0.020400	0.000002	0.000002	0.110702	2.765953	0.006304	2.456495	0.103445	3.444210	0.007882	0.244826	0.003208	1.0040
												0.000710	0.240079	0.072318	2.6265
199613	50.211075	5.343008	23.569944	0.668767	34.022003	0.327357	14.966999	0.007765	0.450505	0.554315	29.183754	0.000003	6 731778	0.000040	1.0410
200507	58.862373	5.336366	23.593978	0.703330	34.202394	0.344200	17.056654	0.006233	0.457651	0.582735	28.327766	0.020001	0.224727	0.007043	2.0744
247982	0.000010 12.185286	0.027794 5.435625	0.020312	0.000002 0.773304	0.000002 36.566004	0.174201	2.914700	0.129189	2.578351 9.473587	0.153855	3.013474	0.011489	0.350035	0.004000	2.1012
723510	0.004708	0.020230	0.000000	0.000002	0.000002	0.100400	2.956159	0.140001	2.005549	0.107333	3.454673	0.012429	0.201172	0.182233	2.1207
												0.033404	0.204333	0.110190	7,1300
207730	83.472745 0.361629	0.071077	23.204688 6.606178	0.845535 0.000002	34.026176	0.414514	37.437254	0.010000	0.485227 2.666623	0.700575	20.000433	0.014417	0.207012	0.110441	1,176
366677	84.008115					0.432728					29.648608	0.03445	6.75560	B. 120000	
		0.029414	8.828134 23.108142	0.000002	8.000002 20.282257		3.848685	0.177750	2.087984 0.499576	0.750007					2.197
.005050	0.557362	0.029748	0.020000	0.000002	0.000002	0.250676	3.883744	0.191045	2.715673	0.225495	3.689739	0.030553	0.272819	0.135014	2.221
												0.037670	0.275776	0.344918	2.2455
375774	05.007542	5.556562 6.636332	23.010000	0.006149	35.433113	0.410002	17.000441	0.012163	0.511500	0.023100	29.468262	0.038823	0.278772	0.150200	2.2591
.200408	0.551253	5.423294 6.636584	22.042021	1.022000	33.004703	0.508153	17.007674 3.163670	0.012020	0.517973	0.027270	29.600000	0.020004	0.201007	0.163917	2.294
867137	0.549279	0.030013	0.025013	B. 000003	0.000002	0.323077	3.218512	0.248563	2.838189	0.243923	3.979526	0.021319	0.284877	0.173000	2.3169
879720	0.547319	0.031021	0.025869	0.000003 1.132912	8.606082 20.262220	0.339953	3.253745	0.263981	2.050695	0.311988	4.011924	0.022464	0.207903	0.183933	2.344
												0.023743	0.201115	0.104318	2.3760
.500331	0.543471	4.931846	22.000270 0.020704	1.190037	9.000002	0.507783	3,325222	0.014015	0.542099	0.390301	50.178785 6.005851	0.033847	0.204274	0.20000	2.201
	59.643762 0.543569	4.009710	22.428977 0.625762	1,237591	30.017710 0.000002		3.363372	0.015383	0.540000	0.24009		0.021212	0.207453	0.235797	2.423
.0022044						0.200876					4.138241				
020363	0.530670	0.031678	6.625700 22.232934	0.000003	0.000002	0.410334	3.307732	0.329390	2.000200	0.388833	4.100024	0.027730	0.300644	0.326844	2.4477
												0.020120	0.303047	0.238679	2.4730
.021004	63.378834	4.453517	22.462124	1,365272	37.061790	0.673588	16.516326	0.017137	0.566257	1.130450	30.002713	0.020122	0.707004	0.249499	2,4991
638382	61.917367	4.274387	22.410095	1.400017	37.202036	0.003152	10.505040	0.017738	0.571995	1.100409	30.713146	0.033323	6.335538	6.761607	1 1 1 1 1 1
031000	0.032151 62.018745	0.032009	0.023530	0.000003	0.000002 27-473543	0.504500	3.544053 18.755899	0.408230	3.163087	0.471840	4.351343	0.033399	0.333440	0.272889	2.5519
												0.034870	0.300000	0.204000	2.0777
726375	63.354682	2.752563	22.263581	1.542511	37.661462	0.755390	18.778784	0.010502	0.588929	1.277616	33.626410	0.033333	A 333676	6 797747	1 6613

PRELIMINARY RESULTS



PRELIMINARY SUMMARY

- ► Able to simulate a model system with primary substrate of fiber, nine subsequent substrates/metabolites, four biomass functional groups with up to ten subdivisions per group.
- ▶ We investigated how the colon microbiota composition varies as a result of three factors: (1) the total amount of fiber consumed, (2) the number of meals in which the fiber is distributed, and (3) the length/intensity of the meal.
 - ► The length of meal (15 minutes versus 30 minutes) has limited effect on the measured output.
 - Difference between measured output generated through a high-fiber diet and low-fiber diet simulation is amplified when meals are less frequent, and diminished when meals are consumed more frequently.

PRELIMINARY SUMMARY

- ► Measurements of state variables vary along the length of the colon, suggesting that using single (CSTR-type) lumped assumptions may be in adequate.
- Overall system performance, judging how the anaerobic digestion process proceeds, during a period of distress is tempered by having a diverse microbial community present. However, the composition of the microbial community after a distress/perturbation period is often not the same as it was prior to that period.

$$\partial_{t}A_{1} + \bar{v}_{l}\partial_{x}A_{1} = -Y_{a}\kappa_{a}\frac{A_{1}X_{1}}{K_{a} + A_{1}} - \frac{\gamma_{3,a}}{V_{l}}(A_{1} - A_{2}), \qquad (6)$$

$$\partial_{t}X_{1} + \bar{v}_{l}\partial_{x}X_{1} = Y_{x}\mu_{f}(S_{1}, X_{1}) - \left(\kappa_{a}\frac{A_{1}}{K_{a} + A_{1}} + \kappa_{d} + \gamma_{1,1}\right)X_{1}$$

$$+ \left(\frac{V_{m}}{V_{l}}\right)\gamma_{4,1}X_{2}, \qquad (7)$$

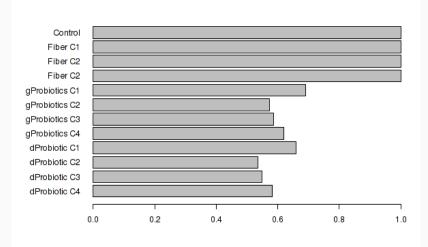
$$\partial_{t}A_{2} = -Y_{a}\kappa_{a}\frac{A_{2}X_{2}}{K_{a} + A_{2}} + \frac{\gamma_{3,a}}{V_{m}}(A_{1} - A_{2}), \qquad (8)$$

$$\partial_{t}X_{2} = Y_{x}\mu_{f}(S_{2}, X_{2}) - \left(\kappa_{a}\frac{A_{2}}{K_{a} + A_{2}} + \kappa_{d} + \gamma_{4,1}\right)X_{2}$$

$$+ \left(\frac{V_{l}}{V_{m}}\right)\gamma_{1,1}X_{1}, \qquad (9)$$

For so	oluble components										
	Component i	1	2	3	4	5	6	7	8	9	Kinetic Rate
Pr	Process	S ₁	S ₂	S ₃	S ₄	S ₅	S ₆	S ₇	S ₈	S ₉	
1	Hydrolysis	Y _{1,1}									$\phi_1(c)$
2	Glucose utilization	-1	Y2,2	Y3,2	Y _{4,2}	Y _{5,2}	Y _{6,2}		Y8,2	Y _{9,2}	$\phi_2(c)$
3	Lactate utilization		-1	Y3,3	Y _{4,3}	Y _{5,3}	Y _{6,3}		Y _{8,3}	Y _{9,3}	$\phi_3(c)$
4	Homoacetogenesis			-1	Y4,4				Y8,4	Y9,4	$\phi_4(c)$
5	Methanogenesis			-1				Y _{7,5}	Y _{8,5}	Y _{9,5}	$\phi_5(c)$
For p	articulate components								_		
	Component i	10	11	12	13	14	15	Kinetio	Rate		
J	Process	11	A ₁	<i>x</i> ₁	<i>X</i> ₂	Х ₃	X_4		la la	Y.,	
1	Hydrolysis	-1						$\phi_1(c)$	$= \kappa_1 \frac{r_1}{K_1 X}$	1+/1	
2	Glucose utilization			Y _{11,2}				$\phi_2(c)$	$= \kappa_1 \frac{I_1}{K_1 X}$ $= \kappa_2 \frac{S_1}{K_2}$ $= \kappa_3 \frac{S_2}{K_3}$ $= \kappa_4 \frac{S_3}{K_3}$	X ₁ ⊢S ₁	
3	Lactate utilization				Y _{12,3}			$\phi_3(c)$	$= \kappa_3 \frac{s_2}{\kappa_3}$	FS ₂	
4	Homoacetogenesis					Y _{13,4}		$\phi_4(c)$	$= \kappa_4 \frac{s_3}{\kappa_3}$	<u>^3</u> +S₃ v.	
5	Methanogenesis						Y _{14,5}	$\phi_5(c)$	$= \kappa_5 \frac{53}{K_5}$	<u>^4</u> ⊧S ₃ ^I рН	I_nH
								with Ip	$H = \begin{cases} ex_1 \\ 1 \end{cases}$	p(-3(pH	$\frac{1-pH_U}{U-pH_L})^2$) if pH $< pH_U$, if pH $\ge pH_U$
6	Decay of X ₁			-1				$\phi_6(c)$	$= \kappa_{6,1} X_1$		
7	Decay of X ₂				-1			$\phi_7(c)$	$= \kappa_{7,1} X_2$		
8	Decay of X ₃					-1		$\phi_8(c)$	$= \kappa_{8,1} X_3$	3	
9	Decay of X_4						-1	$\phi_9(c)$	$= \kappa_{9,1} X_{2}$	+	
10	SAT		Y _{11,10}	-1				$\phi_{A,1}(c)$:)		

Sim No.	Category	Case	Description
1	Control	1	compuGUT is initially simulated for 14 days with standard diet from default initial conditions. After initial period, system receives 2.5 mL of targeted antibiotic ever 4 hours for 5 days. After day 20, system is simulated at standard operating conditions for 312 days (recovery).
2	Fiber	1	Same as control, except following antibiotic treatment (day 20) fiber intake is increased to 40 g per meal for 10 days
3		2	Same as control, except following antibiotic treatment (day 20) fiber intake is increased to 80 g per meal for 10 days
4		3	Same as control, except following antibiotic treatment (day 20) fiber intake is increased to 40 g per meal for 20 days
5	Competitive Culture	1	except following antibiotic treatment (day 20) - 2 g/d of a generic probiotic supplement are consumed for a total period of 10 days
6		2	Same as control, except following antibiotic treatment (day 20) - 4 g/d of a generic probiotic supplement are consumed for a total period of 10 days
7		3	Same as control, except following antibiotic treatment (day 20) - 2 g/d of a generic probiotic supplement are consumed for a total period of 20 days
8		4	Same as control, except following antibiotic treatment (day 20) - a single 40 g dosage of a generic probiotic supplement is consumed
9	Flora re- compliment	1	Same as control, except following antibiotic treatment (day 20) - 2 g/d of a probiotic supplement designed to resemble a pre-treatment flora are consumed for a total period of 10 days
10		2	Same as control, except following antibiotic treatment (day 20) - 4 g/d of a probiotic supplement designed to resemble a pre-treatment flora are consumed for a total period of 10 days
11		3	Same as control, except following antibiotic treatment (day 20) - 2 g/d of a probiotic supplement designed to resemble a pre-treatment flora are consumed for a total period of 20 days
12		4	Same as control, except following antibiotic treatment (day 20) - a single 40 g dosage of a probiotic supplement designed to resemble a pre-treatment flora is consumed



ANTIMICROBIAL SUMMARY

- ► Simulation results suggest:
 - Dynamic effect of antimicrobial treatment varies between colon locations
 - ► Low dosages and short duration treatment regimes, though ineffective in eliminating the targeted biomass strain, alter the long-term composition of the microflora if there is no external intervention.
 - ► Probiotic-type intervention may be an effective method to improve rate of recovery after an unwanted shift in flora composition.

CONCLUDING REMARKS

The compuGUT is very far from being a finished product. What has been demonstrated might best be described as foundational work. However, laying this foundation, the compuGUT, is an important initiative in promoting a sustainable modeling-experimental iterative approach, pushing forward for detailed understanding of the gut microbiota, its interactions, and impacts on health.

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For complete source see http://compugut.sourceforge.net.

